REMARKS

Claim 5 has been amended to specify that the exon to be amplified is any one of exons 1-6 and 8-15.

Claim 6 has been amended to delete a primer pair to be consistent with claim 5 as amended.

New claims 11-17 have been added, and are similar to claims 5-10. New claim 11 is directed to the method for detecting a mutation which causes or is associated with long QT syndrome by amplifying any two or more of exons 1-15. Support for this amendment can be found, for example, in paragraphs 49, 163, 192 and 193 of the specification. New claims 12-16 are dependent on new claim 11 and are similar to claims 6-10. New claim 17 is dependent on new claim 11 and specifies the amplification of all 15 exons.

It is submitted that these amendments do not constitute new matter, and their entry is requested.

Restriction Requirement

The Examiner required restriction among 18 Groups in which each group consisted of a single primer pair set forth in claim 6. Applicants affirm their provisional election of Group III, claims 5-10 (SEQ ID NOs:60 and 61). This election was made with traverse. Applicants submit that this restriction is improper.

Applicants initially note that this restriction is not proper with respect to claims 5, 7 and 9 which do not specify pairs of primers as set forth in claims 6, 8 and 10. Thus, Applicants submit that at best, the proper action should have been an election of species. Furthermore, claim 6 is a Markush claim, which also suggests that an election of species and not a restriction requirement was the proper course of action by the Examiner. With an election of species, once one species is determined to be patentable then additional species should be examined. Applicants submit that the Examiner should examine all of the species of primer pairs set forth in claim 6.

In addition, Applicants direct the Examiner's attention to Keating et al. (US 6,207,383) which was cited in the current Office Action. Claim 9 of Keating et al. is directed to a pair of nucleic acids selected from the group consisting of the very primers set forth in claim 6 of the present application.

Since these nucleic acids, e.g., primers in the present application, are claimed in the '383 patent, the Patent Office has already determined that they are patentable. Because the primers have already been determined to be patentable, a method that utilizes these primers must also be patentable. Since these primers have already been found to be patentable, there can be no undue burden on the Examiner to consider all of the primer pairs with respect to the claims of the present application.

Furthermore, even if a restriction requirement may arguably be proper, Applicants submit that it would not be proper under the present facts. The Examiner has stated on page 2 of the outstanding Office Action that the primer pairs of the present claims are distinct because they have unique nucleotide sequences. However, not only must the primer pair sequences be distinct, but a search and examination of all sequences together must place a burden on the Examiner that would rise to the level of "undue." Applicants disagree with the Examiner's position that such a search would result in an undue burden on the Examiner despite the fact that all of the primer pair sequences are classified together. Applicants support their position with the following reasons and arguments set out below.

There are two criteria for a proper requirement for restriction between patentably distinct inventions: 1) the inventions must be independent or distinct as claimed; and 2) there must be a serious burden on the Examiner if restriction is not required. See MPEP § 803. Examiner's must provide reasons and/or examples to support their conclusions. For purposes of the initial requirement, a serious burden on the Examiner may be *prima facie* shown if the Examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by Applicants. Insofar as the criteria for restriction practice relating to Markush-type claims is concerned, the criteria are set forth in MPEP § 803.02. See MPEP § 803. According to the MPEP, if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent

and distinct inventions. In such a case, the Examiner will not require restriction. See MPEP § 803.02.

Concerning the elected claims of the present application, Applicants agree that the various primer pairsequences may be distinct from each other. However, as stated in the MPEP, as discussed above, distinctness alone is not enough to require a restriction. There must also be a serious burden upon the Examiner. In the absence of such a burden, the Examiner must examine all of the claims (or in this case, it is urged that all of the primer pair sequences should be examined). It is urged that the burden of examining all of the primer pair sequences of the claims is not a serious one, and that the burden of examining all of these primer pair sequences requires no additional searching beyond what the Examiner would have to search in order to examine claim 5.

The examination entails various aspects. **First** is a decision concerning utility under 35 U.S.C. §101. Although each primer pair sequence being claimed is distinct, they are all related because they all are primers for amplifying the various exons of HERG. Consequently, a decision concerning utility will be identical for all of the primer pair sequences, and there is no added burden of examining all of the primer pair sequences as compared to examining only a single primer pair sequence.

The **second aspect** of examination is whether the provisions of the various paragraphs of 35 U.S.C. § 112 have been met. In general, and in this case, this means reviewing the application and claims for compliance with the provisions of paragraphs 1 and 2 of § 112. As for the enablement aspect as found in paragraph 1 of § 112, all of the primer pair sequences are related because they are are all primers for amplifying the various exons of HERG. Since no basis for distinguishing between the enablement of one primer pair sequence vs. another primer pair sequence has been set forth, it is presumed that all of the listed primer pair sequences will be treated equally. Again, this means that only a single decision needs to be made concerning all of the primer pair sequences. Therefore, this aspect of the examination will not be a serious burden if all primer pair sequences are examined, vs. only one of the primer pair sequences.

Concerning paragraph 2 of § 112, this involves the wording of the claims. Any objections to the language of the claims would be the same regardless of which primer pair sequence was being examined. Therefore, there is no increase in the burden concerning 35 U.S.C. § 112, second paragraph, if all primer pair sequences are examined.

The **third aspect** of examination is a review of prior art to determine whether the claims are anticipated or obvious. There are two aspects of such a search, which include a review of the prior art literature and patents, as well as a computer search for the relevant sequences. Both the literature to be reviewed and the computer search will be identical for all of the primer pair sequences. All of the claimed primer pair sequences, although having different nucleotide sequences, correspond to the same gene (HERG) and all are claimed to have the same utility. Indeed, the Examiner's search for primer pair sequences in view of claim 5 will encompass all of the specifically listed primer pair sequences, and the search will be one search identical for all.

The elected subject matter of this application relates to primer pair sequences of HERG and Applicants assert that a search for a primer pair sequence covered by claim 5 would be coextensive with a search for all claimed primer pair sequences and not place an undue burden on the Examiner. Furthermore, as noted above, all of the primer pairs have already been determined by the Patent Office to be patentable.

Consequently, it is submitted that the only reason for requiring a selection of primer pair sequences is because they are distinct from each other. But as explicitly stated in MPEP § 803, the inventions must be distinct and there must be a serious burden on the Examiner. MPEP § 803.02 states that if a search and examination of an entire claim can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. As urged above, it is submitted that examination of all of the primer pair sequences will not impose a serious burden, especially since the Patent Office has already determined that the sequences are patentable.

Applicants assert that, consistent with the established Office policy recited in MPEP §803.04 and referred to above, all of the primer pair sequences should be examined together. Accordingly,

Applicants respectfully request reconsideration and withdrawal of the Restriction Requirement set forth in the current Office Action.

Claim Objection

Applicants note the Examiner's objection to claim 6. In view of the above remarks concerning the restriction requirement, Applicants submit that this objection is not appropriate and should be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected claim 5 under 35 U.S.C. § 102(b) as being anticipated by Keating et al. (US 5,599,673). Keating et al. discloses a genomic characterization of HERG. According to this characterization, HERG comprises three introns (see Figure 9) and thus at best four exons. Keating et al. discloses several primers for the amplification of HERG. The present application discloses that HERG contains 15 exons. Keating et al. discloses that the HERG coding sequence was discovered by Warmke and Ganetzky (see column 2, lines 54 *et seq.* of Keating et al.). Keating et al. discloses several primers that could be used for amplification of HERG. See Table 1 of Keating et al. Applicants have mapped the primer sequences disclosed by Keating et al. as well as the several of the intron positions disclosed in the present application. A copy of the GenBank accession for HERG showing the location of the Keating et al. primers and intron positions disclosed in the present application is attached for the convenience of the Examiner. An analysis of these primers with respect to the HERG coding sequence establishes that all of the primers except those located in the introns are within the coding sequence of HERG, and their use would not amplify an entire exon and no other exon or portion thereof. This same analysis establishes that the primers for intron I (4L) and intron II (12R) may be capable of amplifying the entire exon 7 and no other exon or portion thereof. In view of this disclosure in Keating et al., Applicants have amended claim 5 such that it does not include exon 7. Thus, Applicants submit that Keating et al. does not anticipate claim 5 as amended.

In view of the above amendments and remarks, it is submitted that the Keating et al. does not anticipate the claimed invention. Withdrawal of this rejection is requested.

Because Keating et al. does not disclose the amplification of any two or more exons or all of the exons of HERG, Applicants submit that new claims 11-17 are not anticipated by Keating et al.

Rejection for Obviousness-Type Double Patenting

The Examiner has rejected claims 5-10 for obviousness-type double patenting over claims 3-8, 10, 15 and 16 of U.S. Patent No. 6,207,383, although she has mischaracterized these claims as anticipating the currently claimed invention. Applicants submit that the claims of the '383 patent are not identical to the claims of the present application, and thus there is no same-type double patenting. Thus, Applicants submit that the Examiner's initial characterization of this rejection as being an obviousness-type double patenting rejection is the more proper characterization. In response to this rejection, Applicants are submitting concurrently herewith a Terminal Disclaimer.

In view of the Terminal Disclaimer, it is submitted that this rejection has been obviated. Withdrawal of this rejection is requested.

Conclusions

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes and reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,
ROTHWELL, FIGG, ERNST & MANBECK, p.c.

By _____

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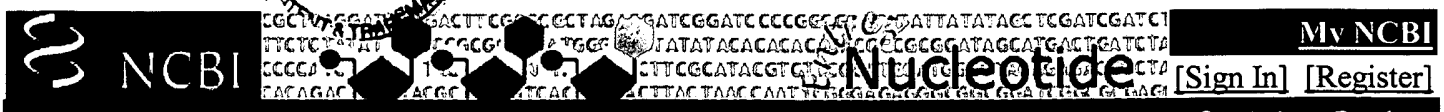
Attachment: GenBank printout for U04270 showing primers and intron positions (3 pages)



1: U04270. Reports Human putative po...[gi:487737]

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DEFINITION  Human putative potassium channel subunit (h-erg) mRNA, complete
            cds.
ACCESSION   U04270
VERSION     U04270.1  GI:487737
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 184 to 3663)
  AUTHORS   Warmke,J.W. and Ganetzky,B.
  TITLE     A family of potassium channel genes related to eag in Drosophila
            and mammals
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 91 (8), 3438-3442 (1994)
   PUBMED   8159766
REFERENCE   2  (bases 1 to 4070)
  AUTHORS   Warmke,J.W.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-DEC-1993) Jeffrey W. Warmke, Genetics and Molecular
            Biology, Merck Research Laboratories, 126 East Lincoln Avenue, P.O.
            Box 2000, Rahway, NJ 07065, USA
FEATURES             Location/Qualifiers
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                     KTFRLKLPALLALTARESSVRSGGAGGAGAPGAVVVDVDLTPAAPSSESLALDEVTAM
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TSTSPLLPVSPLPTLTLDSLSQVSQFMACEELPPGAPELPQEGPTRRLSLPGQLGALT
SQPLHRHGSDPGS"

ORIGIN [***Showing Table 1 primers from '673 patent and partial intron locations from USSN 10/696,708***]

```
       1 acgcggcctg ctcaggcctc cagcggccgg tcggagggga ggcgggaggc gagcgaggac
      61 ccgcgcccgc agtccagtct gtgcgcgccc gtgctcgctt ggcgcggtgc gggaccagcg
     121 ccggccaccc gaagcctagt gcgtcgccgg gtgggtgggc ccgcccggcg ccatgggctc
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     241 cgcaagtttg agggccaga↓g ccgtaagttc atcatcgcca acgctcgggt ggagaactgc
     301 gccgtcatct actgcaacga cggcttctgc gagctgtgcg gctactcgcg ggccgaggtg
     361 atgcagcgac cctgcacctg cgacttcctg cacgggccgc gcacgcagcg ccgcgctgcc
     421 gcgcagatcg cgcaggcact gctgggcgcc gaggagcgca aagtggaaat cgccttctac
               intron 2
     481 cggaaagatg↓ ggagctgctt cctatgtctg gtggatgtgg tgcccgtgaa gaacgaggat
     541 ggggctgtca tcatgttcat cctcaatttc gaggtggtga tggagaagga catggtgggg
                                                              intron 3
     601 tccccggctc atgacaccaa ccaccggggc ccccccacca gctggctggc cccag↓gccgc
     661 gccaagacct tccgcctgaa gctgcccgcg ctgctggcgc tgacggcccg ggagtcgtcg
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    1081 ccgcgccacg ccagcaccg↓g ggccatgcac ccactgcgca gcggcttgct caactccacc
    1141 tcggactccg acctcgtgcg ctaccgcacc attagcaaga ttccccaaat caccctcaac
    1201 tttgtggacc tcaagggcga ccccttcttg gcttcgccca ccagtgaccg tgagatcata
                                                          intron 5
    1261 gcacctaaga taaaggagcg aacccacaat gtcactgaga aggtcaccca g↓gtcctgtcc
                           1L
    1321 ctgggcgccg acgtgctgcc tgagtacaag ctgcaggcac cgcgcatcca ccgctggacc
    1381 atcctgcatt acagcccctt caaggccgtg tgggactggc tcatcctgct gctggtcatc
                                                      2L
    1441 tacacggctg tcttcacacc ctactcggct gccttcctgc tgaaggagac ggaagaaggc
    1501 ccgcctgcta ccgagtgtgg ctacgcctgc cagccgctgg ctgtggtgga cctcatcgtg
                                                          3L        7R
    1561 gacatcatgt tcattgtgga catcctcatc aacttccgca ccacctacgt caatgccaac
    1621 gaggaggtgg tcagccaccc cggccgcatc gccgtccact acttcaaggg ctggttcctc
                         8R                                        intron 6*
    1681 atcgacatgg tggccgccat ccccttcgac ctgctcatct tcggctctgg ctctgaggag↓
    1741 ctgatcgggc tgctgaagac tgcgcggctg ctgcggctgg tgcgcgtggc gcggaagctg
              5L        10R
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1801 gatcgctact cagagtacgg cgcggccgtg ctgttcttgc tcatgtgcac ctttgcgctc
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                11R
1921 gactcacgca tcggctggct g cacaacctg ggcgaccaga taggcaaacc ctacaacagc
                  6L
1981 agcggcctgg gcggcccctc catcaaggac aagtatgtga cggcgctcta cttcaccttc
2041 agcagcctca ccagtgtggg cttcggcaac gtctctccca acaccaactc agagaagatc
                                intron 7*
2101 ttctccatct gcgtcatgct cattggct↓cc ctcatgtatg ctagcatctt cggcaacgtg
                                                        13R
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2221 gtgcgggagt tcatccgctt ccaccagatc cccaatcccc tgcgccagcg cctcgaggag
                                                      intron 8
2281 tacttccagc acgcctggtc ctacaccaac ggcatcgaca tgaacgcg↓gt gctgaagggc
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           16L**                                          15L**
2401 tgcaaaccct tccgaggggc caccaagggc tgccttcggg ccctggccat gaagttcaag
2461 accacacatg caccgccagg ggacacactg gtgcatgctg gggacctgct caccgccctg
2521 tacttcatct cccggggctc catcgagatc ctgcggggcg acgtcgtcgt ggccatcctg
  intron 9*
2581 g↓ggaagaatg acatctttgg ggagcctctg aacctgtatg caaggcctgg caagtcgaac
2641 ggggatgtgc gggccctcac ctactgtgac ctacacaaga tccatcggga cgacctgctg
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                  intron 10
2761 ttcaacctgc gagat↓accaa catgatcccg ggctcccccg gcagtacgga gttagagggt
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2881 gagcagccag gggaggtgtc ggccttgggg ccgggccggg cgggggcagg gccgagtagc
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4021 atgaagatgc tgatgactat gaataataaa taattatcct gaggagaaaa
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* Introns 6, 7 and 9 correspond to Introns I, II and III of the '673 patent, respectively (Intron I contains 4L and 9R primers, intron II contains 12R primer and intron III contains 14R primer)

** 16L and 15L are based on primer sequence in Table 1 of '673 patent and not position